

LAWYERS

Davis Wright Tremaine LLP



ANCHORAGE BELLEVUE LOS ANGELES NEW YORK PORTLAND SAN FRANCISCO SEATTLE SHANGHAI WASHINGTON, DC

JANE E. R. POTTER, PH. D.
Direct (206) 628-7650
janepotter@dwt.com2600 CENTURY SQUARE
1501 FOURTH AVENUE
SEATTLE, WA 98101-1688TEL (206) 622-3150
FAX (206) 628-7699
www.dwt.comRECEIVED
CENTRAL FAX CENTER

MAR 08 2005

FACSIMILE TRANSMITTAL

Date: March 8, 2005

Re: U.S. Patent No.: 6,803,453 B1
Issue Date: October 12, 2004
First Named Inventor: Mary E. Brunkow
Attorney Docket No.: 60117-32

SEND TO:

NAME	FIRM/COMPANY/CONFIRMATION NO.	FAX NUMBER
Examiner Patrick J. Nolan	USPTO	1-703-472-9306

FROM:

Jane E. R. Potter Telephone: (206) 628-7650 Fax: (206) 628-7699

NUMBER OF PAGES (including cover page): 5

Floor Sent From: _____ Time Sent: _____ AM PM Operator: _____

RETURN TO SENDER: VIA INTRAOFFICE MAIL ☐ WILL PICK UP ☒ EXTENSION: 7560

COMMENTS:

Dear Mr. Nolan,

Pursuant to our telephone discussion regarding the numerous printing errors, attached for your information is a copy of the Request for Reprinting of Patent.

With best regards,

Jane E. R. Potter, Registration No. 33,332

THE WRITTEN MESSAGE TRANSMITTED HEREBY IS FOR THE EXCLUSIVE USE OF THE ADDRESSEE AND CONTAINS CONFIDENTIAL, PRIVILEGED AND NONDISCLOSABLE INFORMATION. IF THE RECIPIENT OF THIS MESSAGE IS NOT THE ADDRESSEE, OR A PERSON RESPONSIBLE FOR DELIVERING THE MESSAGE TO THE ADDRESSEE, SUCH RECIPIENT IS PROHIBITED FROM READING OR USING THIS MESSAGE IN ANY WAY. IF YOU HAVE RECEIVED THIS MESSAGE BY MISTAKE, PLEASE NOTIFY JESSICA GAUNT @ (206) 628-7560 IMMEDIATELY AND DESTROY THE FACSIMILE MESSAGE.

IF YOU DO NOT RECEIVE ALL PAGES OF THIS TRANSMISSION,

PATENT

I hereby certify that on the date specified below, this correspondence is being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

March 8, 2005

Date



Jessica Gaunt

**RECEIVED
CENTRAL FAX CENTER**

MAR 08 2005

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors : Mary E. Brunkow et al.
Patent No. : 6,803,453 B1
Issue Date : October 12, 2004
Title : ANTIBODIES ASSOCIATED WITH ALTERATIONS IN BONE DENSITY

Docket No. : 60117-32

Date : March 8, 2005

Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR REPRINTING OF PATENT

Sir:

A detailed review of U.S. Patent No. 6,803,453, which issued on October 12, 2004, has shown that it contains more than 270 individual errors and entire word substitutions or deletions. Only nine of the errors in the printed version of the patent correspond to minor typographical errors in the application as filed. As a result, at least 260 changes are the responsibility of the Patent Office. Many of the errors and changes significantly alter the meaning of terms in the patent, and would lead readers to miss important content. For example, in several cases, the word "epitope" was replaced with "epitome." "Epitope" is an important term in this patent because it defines an immunological construct. In contrast, the word "epitome" is meaningless in that context as that word means "a brief summary" or "an ideal example." The name of the disease

to which the invention relates, sclerosteosis, is spelled incorrectly on multiple occasions. This would preclude a word search of the text by someone using the Patent Office's own database to find relevant patents.

The inaccurate text in Examples 2-9 at columns 41 through 49 is of particular concern as the Examples now contain an inordinate number of technical errors, including errors in the oligonucleotide sequences. These are unacceptable, as correct oligonucleotide sequences are required for a person of ordinary skill in the art to practice the invention. Unlike some word substitutions, errors in DNA sequences would not be obvious from a reading of the text. Many errors are also found in the technical terms, names of compounds used to practice the experiments, and authors of cited references. Unlike simple typographical errors, such errors clearly are not self-evident from a reading of the text.

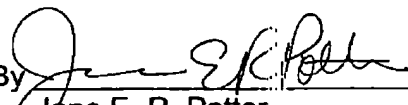
A few examples are as follows. In one paragraph (column 35, lines 53-67) the word "transgenic" appears three times, but on each appearance it is incorrectly, and inconsistently, spelled: at line 54, *transcience*; at line 58, *transonic*; and at line 60, *transgress*. If one were searching the Patent Office records using the key word "transgenic" its accurate contextual use in this patent would not be found. Other examples in which meaningless words are substituted include "its" for patients (col. 2, line 30); "smudgy" for strategy (col. 2, line 49); "polygonal" for polyclonal (col. 28, line 33); "sexes" for secretes (col. 29, line 11); "misinformation" for misincorporation (col. 32, line 14); "son" for expression (col. 39, line 3); and "purificanon" for purification (col. 42, line 28). This is just a very small but representative sample of the numerous changes in terms and words. In many cases words are omitted altogether.

Applicants respectfully but strongly submit that the excessive number of errors present in this patent cannot effectively be rectified by a Certificate of Correction. Even with a list of corrections at hand, a person reading the patent would have an enormous burden when trying to understand the text, particularly for those paragraphs that have 5, 10, or more separate errors. Given the sheer number of corrections required, and the technical significance of the incorrect words and polynucleotide sequences in the context of understanding the invention, applicants request that the Patent Office re-print the patent rather than issue a Certificate of Correction. Issuance

of the patent in its current condition reflects badly on the high quality of the Patent Office. The invention and the patent in which it is claimed reflect an extensive investment of time by both the applicants and the Examiner. Applicants expect that this patent will be referred to and read often and it is an embarrassment.

Filed herewith is a marked-up copy of the patent, showing the errors, changes and omitted words.

Respectfully submitted,
Mary E. Brunkow et al.
DAVIS WRIGHT TREMAINE LLP

By 
Jane E. R. Potter
Registration No. 33,332

2600 Century Square
1501 Fourth Avenue
Seattle, WA 98101-1688
Phone: (206) 628-7650
Facsimile: (206) 628-7699



US006803453B1

(12) **United States Patent**
Brunkow et al.

(10) Patent No.: **US 6,803,453 B1**
 (45) Date of Patent: **Oct. 12, 2004**

(54) **ANTIBODIES ASSOCIATED WITH ALTERATIONS IN BONE DENSITY**

(75) Inventors: Mary E. Brunkow, Seattle, WA (US); David J. Galas, Mercer Island, WA (US); Brian Kovacevich, Renton, WA (US); John T. Mulligan, Seattle, WA (US); Bryan W. Paepker, Seattle, WA (US); Jeffrey Van Ness, Seattle, WA (US); David G. Winkler, Seattle, WA (US)

(73) Assignee: **Darwin Discovery Ltd., Bothell, WA (US)**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 151 days.

(21) Appl. No.: **09/668,021**

(22) Filed: **Sep. 21, 2000**

Related U.S. Application Data

- (62) Division of application No. 09/449,218, filed on Nov. 24, 1999, now Pat. No. 6,395,511.
 (60) Provisional application No. 60/110,283, filed on Nov. 27, 1998.
 (51) Int. Cl.⁷ **C07K 16/00**
 (52) U.S. Cl. **530/388.23; 435/331; 424/184.1; 530/387.1; 530/388.1; 530/388.2; 530/389.2**
 (58) Field of Search **435/331; 424/184.1; 530/387.1, 388.1, 388.2, 388.23, 389.2**

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,453,492 A	9/1995	Bützow et al.	530/413
5,780,263 A	7/1998	Hastings et al.	435/69.1
5,811,238 A	9/1998	Stemmer et al.	435/6
5,830,721 A	11/1998	Stemmer et al.	435/172.1
5,837,458 A	11/1998	Minshall et al.	435/6

FOREIGN PATENT DOCUMENTS

WO	WO 91/13152	9/1991
WO	WO 92/06693	4/1992

OTHER PUBLICATIONS

Colman et al., *Research in Immunology*, vol. 145 pp. 33-36, 1994.*
 Hay et al. (*ATCC Cell Lines and Hybridomas*, 8th ed. 1994; pp. 149, 258, and 428).*

Harlow et al. (*Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988, pp. 141-157.*

Bendayan (*The Journal of Histochemistry and Cytochemistry*, 1995, 43(9): 881-886).*

Bost et al. (*Immunological Investigations*, 1988, 17(6&7): 577-586).*

Birren et al., *EMBL Sequence Database*, Accession No. AC003098, Nov. 14, 1997.

Bonaldo et al., "Normalization and Subtraction: Two Approaches to Facilitate Gene Discovery," *Genome Res.* 6(9):791-1996.

Bonaldo et al., *EMBL Sequence Database*, Accession No. AJ113131, Sep. 4, 1998.

Hillier et al., *EMBL Sequence Database*, Accession No. AA393939, May 19, 1997.

Hsu et al., "The *Xenopus* dorsalizing factor gremlin identifies a novel family of secreted proteins that antagonize BMP activities," *Molecular Cell* 1:673-681, 1998.

Iemura et al., "Direct binding of follistatin to a complex of bone-morphogenetic protein and its receptor inhibits ventral and epidermal cell fates in early *Xenopus* embryo", *Proc. Natl. Acad. Sci. USA* 95:9337-9342, 1998.

Khosla and Riggs, "Concise review for primary-care physicians. Treatment options for osteoporosis," *Mayo Clinic Proc* 70:978-982, 1995.

Riggs, "Overview of osteoporosis," *West J. Med.* 154:63-77, 1991.

* cited by examiner

Primary Examiner—Patrick J. Nolan

(74) Attorney, Agent, or Firm—Seed Intellectual Property Law Group PLLC

(57) **ABSTRACT**

Compositions and methods for increasing bone density using antibodies directed to a novel class or family of TGF- β binding proteins are provided. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases associated with a loss of bone density, for example osteoporosis.

12 Claims, 6 Drawing Sheets

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

☒ BLACK BORDERS

☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

☐ FADED TEXT OR DRAWING

☒ BLURRED OR ILLEGIBLE TEXT OR DRAWING

☐ SKEWED/SLANTED IMAGES

☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS

☐ GRAY SCALE DOCUMENTS

☒ LINES OR MARKS ON ORIGINAL DOCUMENT

☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.